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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/515,276
Filing Date: February 29, 2000
Appellant(s): MONTMINY, MARC R.

Stephen E. Reiter
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed April 27, 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 1-7, 12, and 17 do not stand or fall together with either claims 18-24 and 33, or claims 25-32 and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Herzig et al., "CREB regulates hepatic gluconeogenesis through coactivator PGC-1," Nature, vol 413 (Sept 13, 2001), pp. 179-183.

Mayr et al., "Transcriptional regulation by the phosphorylation-dependant factor CREB," Nature Reviews, vol 2 (Aug 2001), pp. 599-609.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

(I) Claims 1-7, 12, and 17-33 are rejected for lack of written description under 35 U.S.C. § 112, first paragraph.

Claims 1-7, 12, and 17-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. These claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims read on methods of performing indicated functions through administration of any compound that is capable of inhibiting binding between CREB and CREB binding protein (CBP).

The Appellant asserts that there are three groups of claims, each of which stands or falls separately. The Groups are divided as follows: (Group I) Claims 1-7, 12, and 17, drawn to methods of treating diabetes mellitus in an animal through administration of a compound that inhibits CREB/CBP binding; (Group II) claims 18-24, and 33, drawn to methods of modulating glucose metabolism through the administration of the same compounds; and (Groups III) claims

25-32, drawn to methods of inhibiting expression of phosphoenolpyruvate carboxykinase (PEPCK- a protein enzyme involved in the production of glucose) again through the administration of compounds inhibiting CREB/CBP binding. The Appellant asserts that these different sets of claims do not stand or fall together because each set of claims is directed towards methods performing a different function. However, for the purposes of establishing the grounds of rejection, a single statement of the rejection of all claims is sufficient. This is because in each case, the claims are drawn to the use of any compound that inhibits CREB/CBP binding. Because the claims of each of the three Groups involves the use of such compounds, and because this similarity among the claims is also the focal point of the rejection, a single statement of the rejection to all of the methods is appropriate.

As was indicated above, the claims of the three Groups read on methods of performing a function through administration of any compound that is capable of inhibiting binding between CREB and CREB binding protein (CBP). The compounds used in the methods are identified their function of inhibiting CREB/CBP binding. While the claims also indicate that the compounds may be identified by assays used to identify compounds with the function, such identification provides no additional information than the identification of the function alone. Thus, the claims are directed to methods of using compounds identified only by function.

The Court of Appeals for the Federal Circuit has clearly stated that such identification is not sufficient to provide support for the compounds themselves, or for methods of using them. The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the Appellant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. In cases such as this one, where the genus is identified by reference to a function, the functional identification must by "coupled with a known or disclosed correlation between function and structure." In the present case, neither the claims nor the specification provide any identification of a structure that correlates with the claimed function. Because the application provides no structure or other recognizable characteristic of compounds that have the indicated function of inhibiting CREB/CBP binding, and which correlate to that function, the application has not provided adequate written description support for the claimed methods.

(II) Claims 1-7, 12, and 17-33 are rejected for lacking an enabling disclosure under 35 U.S.C. § 112, first paragraph.

Claims 1-7, 12, and 17-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims have been described above.

The claims were rejected for lack of enablement on two grounds. First, the Appellant has not enabled the practice of the claimed invention with any compound that inhibits the binding of CREB and CBP. Second, the claims were rejected because the Appellant had not established that the mechanism of the methods (inhibiting CREB/CBP binding) would be effective in achieving the desired results. It is noted that the second ground of rejection is no longer maintained by the Examiner on the basis that the teachings of Herzig et al. (Nature, 413: 179-83) indicate that the mechanism may be operable. Thus, the arguments in this Examiner's Answer are directed towards the first ground of rejection, that the Appellant has not enabled the use of any compound that inhibits CREB/CBP binding in the claimed methods.

As with the written description rejection above, the Appellant has asserted that the claims should be divided into three separate groups, each of which stands or falls separately. However, while the Appellant has chosen to argue these three Groups of claims separately, the rejection of all of the claims is set for the below. This is because, in each case, the rejection is based on the lack of enablement for the use of any compound with the ability to inhibit CREB/CBP binding. Because each of the claim groups asserted by the Appellant uses such compounds, and because each of the methods involves the same mode of operation (the inhibition of CREB/CBP binding) the general rejection of the three groups is sufficient to illustrate the grounds of rejection.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary,

(2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. Those factors identified as most relevant are used to determine if the Appellant has provided sufficient information to enable those in the art to make and use the claimed invention without undue experimentation.

The factors considered relevant to this rejection in general are the state of the prior art and the nature of the invention, the breadth of the claims, the presence or absence of working examples, the quantity of experimentation necessary, and the predictability of unpredictability in the art. However, the Appellant's discussion of these factors either adds little or nothing over the issues discussed with respect to the other factors to the determination of whether the Appellant has enabled the practice of the claimed invention without undue experimentation.

The nature of the invention and the state of the art.

The art surrounding the claimed invention is directed to the relationship between the interaction between two proteins, and diabetes or its symptoms. The Appellant asserts that they have found a new means by which to treat diabetes mellitus, or to treat symptoms and function that are often associated with the disorder (i.e. the glucose metabolism, and the expression of the protein PEPCK). This means is through the inhibition of binding between the proteins known in the art as CREB and CREB-binding protein (CBP). While, as asserted by the Appellant, the teachings in the art at the time the application was filed demonstrate the relationship between

diabetes mellitus and the indicated body functions, neither the art, nor the application, show that any compounds have been effective in treating glucose metabolism or diabetes through the claimed mechanism. It is further noted that the art and application indicate that a limited number of specific compounds may inhibit CREB/CBP binding were known. See e.g., application, pages 16-17). However, there do not appear to be any teachings in the art establishing that a general class of such compounds was similarly known. Thus, the art and application demonstrate that the art surrounding the claimed methods were relatively new at the time of filing, and the potential benefits of such methods remain unrealized even four years after the filing date.

The breadth of the claims.

The claims are broadly drawn to methods of treating diabetes mellitus or related conditions through the administration of any compound capable of inhibiting CREB/CBP binding. Thus, in order to practice the claimed invention to the full extent as claimed, the Appellant must have provided sufficient information to enable those in the art to practice the claimed methods, i.e. to use any such compound, without undue experimentation. However, the scope of compounds that are asserted to be useful in the claimed invention are not limited to those compounds disclosed in the application. See, pages 15-17. Further, while the Appellant asserts that these compounds each share the functional activity of inhibiting CREB/CBP binding, the specification also indicates that this inhibition need not be direct. Rather, as exemplified by the reference to antibodies inhibiting the phosphorylation of CREB on lines 13-16 of page 16, the Appellant has also included in the claims the use of any compound that may inhibit any other

preliminary process required for CREB/CBP binding. Thus, the claims are broadly drawn to any compound that may inhibit in any manner the binding of CREB to CBP.

The presence or absence of working examples.

In contrast to the breadth of the claims, the application provides only a limited number of suggestions as to what compounds may have the required function. Pages 15-16, cited above. Further, while the Appellant has provided these suggestions, none of the suggested compounds appear to share any common feature, including mode of operation, that would indicate to those in the art what other compounds may also be useful in the claimed methods. Thus, while the Appellant has provided a few examples of compounds that may be effect in the claimed methods, they provide those in the art with little guidance in picking and choosing among the vast array of potential compounds that may also be found to be useful in the claimed method.

It is also noted that the Appellants have demonstrated the microinjection of certain of these compounds directly into cells results in the inhibition of an artificial CREB pathway. There is, however, no direct evidence in the application either that the result is achieved through inhibition of CREB/CBP binding, or that the administration of the compounds would have the desired effects when administered to an organism in vivo.

The predictability or unpredictability of the art.

The art also appears uncertain about the efficacy of the claimed methods. It is noted that post-filing art indicates that the activity of the CREB protein may be associated with certain of the conditions treated in the claimed methods. See, Mayr et al., Nature Reviews 2:599-609; and

Herzig et al., Nature, 13: 179-183. However, even in the Herzig reference, which was published four year after the filing date, merely suggests that the interaction of CREB and CBP "may" be an effective therapy for diabetes, and for the lowering of blood glucose levels (i.e. modulating glucose metabolism). Further, the reference suggests the inhibition of CREB/CBP binding as an alternative to the use of a dominant negative version of the CREB protein, which the reference admits "may not be feasible." Through its teachings, the reference simultaneously supports the assertion that CREB/CBP binding may be an appropriate target for the claimed treatment methods, but also demonstrates uncertainty in the operability of the claimed methods based on uncertainty as to what compounds may ultimately be effective.

With respect to the ability of compounds to inhibit CREB/CBP binding, it is noted only that there does not appear to be any common structural feature associated with the indicated function. In view of this lack of a common feature, it would appear that there is little in the art to enable those in the art to easily determine what compounds may be used in the claimed methods. Because there is little guidance as to what compounds may be used, it would appear that it is unpredictable what compounds would be useful in the claimed methods.

Thus, there is uncertainty both in what compounds may possess the ability to inhibit CREB/CBP binding, and in which, if any, of these compounds may ultimately be found to have therapeutic benefit.

The quantity of experimentation required.

However, while the compounds that may eventually be used appears to be uncertain, the claimed methods read broadly on the use of any compounds with the desired activity. As was

stated above, these compounds have been identified solely by their intended function (inhibition of CREB/CBP binding). The Appellant has asserted that these compounds may be identified both by their function, and through their identification using assays provided in the application. However, while it may be acknowledged that the Appellant in enabled for the use of these assays for the identification of compounds that inhibit CREB/CBP binding, this is not tantamount to stating that the Appellant is enabled for the use of any and all compounds that may eventually be identified through its use. As indicated above, the claims are drawn to the use of any compound that inhibits CREB/CBP binding. Such compounds may be found anywhere in the vast array of potential chemical structures in nature or that may be made by man.

The Appellant has provided little, if any, guidance as to which of these compounds may in fact have the necessary functional activities. In this case, while there may be only a limited and acceptable amount of experimentation required to determine if any one compound would have the required functional activity, the claims are drawn to the use of any compound with the indicated activities. In order to practice the claimed methods to the full scope as claimed, those in the art must be able to identify all such compounds without undue experimentation.

The Appellant has not enabled the practice of the claimed methods without undue experimentation.

Consideration of the above factors indicate that the Appellant is not enabled for the practice of the claimed methods without undue experimentation. The factors indicate that the Appellant has not provided sufficient information to enable the use of any compound that inhibits binding between CREB and CBP. It is conceded that the application sets forth a limited

number of examples of compounds that may be used, and an assay for the identification of further compounds. However, such limited guidance is contrasted with a lack of guidance towards additional operable compounds, the vast array of potentially useful compounds, the unpredictability in the art, and the great breadth of the claims encompassing the use any compound with the requisite activity that has not yet been identified. These factors therefore indicate that the Appellant is not enabled for the use of any compound that inhibits the binding of CREB with CBP. Because the application has not provided sufficient information such that those in the art may practice the claimed methods with any compound that inhibits CREB/CBP binding without undue experimentation, the Appellant has not enabled the practice of the claimed methods.

This rejection is applied equally to the three Groups of claims asserted by the Appellant. This is because each set of claims is directed to the use of compounds with the ability to inhibit CREB/CBP binding. Because the Appellant has not enabled the use of such compounds generally, the Appellant has not enabled the use of such compounds in any of the three method groups.

(11) Response to Arguments

For the above reasons, it is believed that the rejections should be sustained.

(I) The rejection of claims 1-7, 12, and 17-33 for lack of written description support should be affirmed.

Claims 1-7, 12, and 17-33 have been rejected for lack of adequate written description support in the specification. These claims each describe methods of using compounds that inhibit the binding of the protein CREB with the protein referred to as CREB binding protein (CBP). The Appellant has argued that these claims should stand or fall separately in three different groups. Brief, page 8. The Appellant's arguments with respect to these Groups are answered below.

There is insufficient written description support for use of compounds able to inhibit CREB/CBP binding in the methods of claims 1-7, 12, and 17.

With respect to the claims of Group I, claims 1-7, 12, and 17, drawn to methods of using the compounds to treat diabetes mellitus, the Appellant has traversed the rejection on the grounds that "the Examiner has cited no law for the extreme position that the written description for a methods claim requires a chemical structure...which contemplates use of a compound, the identity of which can be determined by methods extensively described and admitted by the Examiner to be enabling, and where exemplary compounds are disclosed in the specification." This argument is not persuasive on its merits for two reasons.

First, while the prior actions do not specifically cite law in support of the rejection of the claims on the basis of identification solely by function; the legal proposition is one supported by the Federal Circuit, for example in the Eli Lilly decision cited above. It is noted that the Eli Lilly decision factually relates to claims drawn to the compounds themselves. However, the Federal Circuit has also applied this rationale to claims drawn to methods of using compounds so identified. See, University of Rochester v G.D. Searle & Co., 69 U.S.P.Q.2d 1886, at 1894 (stating, in response to an attempt to distinguish between the rejection of claims drawn to compounds and methods of using them, that such a distinction is " a semantic distinction without a difference"). Thus, while no specific legal citation has been made of record, the legal analysis in fact supported by the Federal Circuit's decisions of written description issues.

The Appellant also asserts that they have disclosed the structures of certain compounds that may be used in the claimed methods. However, as described above, while the application suggests that the suggested compounds may have the required function, there is no direct evidence that such is the case. Further, even if the suggested compounds had been shown to be useful in the claimed methods, they would not be considered representative of the full scope of the claimed genus, which can read on any compound (including peptides, antibodies, or any other molecules) with the required functional activity. There is no showing that the suggested compounds have any common structural characteristic that correlates with the claimed function, nor is there any illustration of how such compounds may be representative of all of the compounds that may be useful in the claimed methods. Thus, there is no demonstration that the suggested compounds are representative of the full scope of the compounds that may be identified by the indicated assays. In view of this, and the statement by the Federal Circuit that

"one must describe a sufficient variety of species to reflect the variation within the genus" (Eli Lilly, cited above), even if it is accepted that these compounds represent species of the claimed invention, they are not sufficient to provide written description support for the full genus of inventions claimed.

For the reasons above, and the reasons of record, the rejection of claims 1-7, 12, and 17 for lack of adequate written description in support of the claimed inventions should be affirmed.

There is insufficient written description support for use of compounds able to inhibit CREB/CBP binding in the methods of claims 18-24, and 33.

The Appellant traverses the rejection of the claims of Group II, claims drawn to methods of modulating glucose metabolism through inhibiting the binding of CREB to CBP, for substantially the same reasons as indicated above with respect to the claims of Group I. The Appellant argues that the application provides examples of compounds that may be used in the claimed methods, and that such disclosure demonstrates possession of the claimed method. These arguments are not found persuasive for the same reasons as indicated above with respect to the claims of Group I. The suggested compounds share no common structural feature, and thus cannot be said to represent any particular genus of inventions. Further, the claims of this Group are also directed to the use of a genus of compounds identified solely by their function. As was also described with respect to Group I above, such identification is not sufficient to provide written description support for a claimed invention. For these reasons, and the reasons of record, the rejection of claims 18-24, and 33 should be affirmed.

There is insufficient written description support for use of compounds able to inhibit CREB/CBP binding in the methods of claims 25-32.

The Appellant traverses the rejection of the claims of Group III, claims drawn to methods of inhibiting expression of PEPCK through inhibiting the binding of CREB to CBP, for the same reasons as indicated above with respect to the claims of Group II. Brief, pages 143-15. As the arguments presented with respect to the claims of Group II have been answered above, and as no additional arguments have been presented with respect to the claims of Group III, the rejection of these claims should be affirmed for the reasons above, and the reasons of record.

(II) The rejection of claims 1-7, 12, and 17-33 for lack of an enabling disclosure should be affirmed.

In response to the rejections for lack of enablement, the Appellant generally asserts that the claimed inventions are supported by an enabling disclosure, and that, from the teachings in the application, those in the art would be able to practice the claimed methods. The Appellant asserts that the Examiner has failed to make a prima facie case for lack of enablement. The Appellant's arguments in support of their assertion are presented in the form of consideration of several of the Wands factors described above. Because the Examiner is arguing only the rejection based on the use of any compound with CREB/CBP binding inhibition activity, only those arguments directed to this ground of rejection are addressed.

As was indicated above, the Appellant has traversed the rejections of the claims as they apply to three different groups of claims, each comprising claims directed to methods of achieving a different result using the compounds referred to above. The Appellant's arguments with respect to these Groups are answered below.

The application has not enabled to methods of claims 1-7, 12, and 17 (Group I) drawn to methods for the treatment of diabetes mellitus through administration of any compound with CREB/CBP binding inhibition activity.

The Appellant traverses the rejection of the claims 1-7, 12, and 17for lack of enablement for the use of any compound with the ability to inhibit CREB/CBP binding on the basis that the application discloses several examples of such compounds that may be used, and that the application also discloses methods which may be used for the identification of further compounds. Brief, page 17 (section entitled "Nature of the Invention"). The Appellant asserts that because they have provided an assay by which such compounds may be identified, those in the art may readily identify other such compounds without undue experimentation. Brief, pages 25-26 (section entitled "Quantity of Experimentation). This argument however should not be found persuasive.

As was described above, the claims are drawn broadly to any compound that may have the effect of inhibiting CREB/CBP binding. Such compounds are not limited to any particular structure, or even to any particular mode of operation. However, in contrast to the breadth of the claims, the application provides only a limited set of suggested compounds that may have the required function, and provides an assay which the Appellant invites those in the art to use to identify other compounds. See, above. No other guidance as to what compounds may also have the required activity is provided. There is no suggestion as to what structural or other features, beyond the functional activity, those in the art could use to determine if a particular compound would be useful in the claimed methods. Thus, those in the art would have to find for themselves the full scope of compounds that may be used to inhibit CREB/CBP binding, and determine which of these is would be effective in achieving therapeutic effects in vivo. In view of the limited teachings, the breadth of the claims, and the vast array of potential compounds that would have to be screened in order to practice the claimed invention to its full extent, there is insufficient information to allow those in the art to so practice the claims without undue experimentation.

In traversal, the Appellant has merely asserted that those in the art would be able to easily identify such other compounds. There is no demonstration that the suggested compounds are, in fact, effective at achieving in vivo results, nor any identification of compounds actually identified using the indicated assays. The Appellant assertions are therefore unsupported arguments. Such arguments, in absence of evidence, are not sufficient to overcome a rejection. See e.g., In re Schulze, 145 U.S.P.Q. 716, 718 (CCPA 1965); supported more recently by In re Geisler, 43 U.S.P.Q. 2d 1362 (Fed. Cir. 1997). Therefore, in view of the discussion above, and

the lack of evidence by the Appellant to the contrary, the rejection of the claims 1-7, 12, and 17 for lack of enablement for the use of any compounds that inhibit CREB/CBP binding should be affirmed.

The application has not enabled to methods of claims 18-24, and 33 (Group II) drawn to methods for the modulation of glucose metabolism through administration of any compound with CREB/CBP binding inhibition activity.

The Appellant traverses the rejection of these claims by asserting that the Examiner has presented no grounds of rejection specifically targeted to methods of modulating glucose metabolism. This argument is not found persuasive because, as was pointed out in the grounds for rejection section, each of the three groups of claims is rejected for the same reason: the Appellant has not enabled the use of any compound that inhibits CREB/CBP binding. The rejection of the claims on this basis is clearly set forth above, as are the answers to the Appellants traversal of the rejection with respect to the claims of Group I. As the Appellant has presented no additional arguments in traversal, the rejection should be affirmed for the reasons above, and the reasons of record.

The application has not enabled to methods of claims 25-32 (Group III) drawn to methods for the inhibition of PEPCK expression through administration of any compound with CREB/CBP binding inhibition activity.

The Appellant traverses the rejection of these claims for the same reasons as argued with respect to the claims of Group II above. The arguments in traversal of the rejection have been

adequately answered above. For those reasons, and the reasons of record, the rejection should be affirmed.

In view of the above, the rejection of all of claims 1-7, 12, and 17-33 for lack of written description, and for lack of enablement should be affirmed.

Respectfully submitted,

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August 6, 2004

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